

From the INTERNATIONAL BUREAU

**PCT**

NOTIFICATION OF TRANSMITTAL  
OF COPIES OF TRANSLATION  
OF THE INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY  
(CHAPTER I OR CHAPTER II  
OF THE PATENT COOPERATION TREATY)  
(PCT Rules 44bis.3(c) and 72.2)

To:

SIKs, & Co.  
8th Floor, Kyobashi-Nisshoku Bldg., 8-7, Kyobashi  
1-chome, Chuo-ku Tokyo  
1040031  
JAPON

Date of mailing ( <i>day/month/year</i> ) 28 September 2006 (28.09.2006)	
Applicant's or agent's file reference A55037H	<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/JP2005/002402	International filing date ( <i>day/month/year</i> ) 17 February 2005 (17.02.2005)
Applicant YAMAGAMI, Satoru et al	

**1. Transmittal of the translation to the applicant.**

The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

**2. Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

**3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Yoshiko Kuwahara

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference A55037H	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/JP2005/002402	International filing date ( <i>day/month/year</i> ) 17 February 2005 (17.02.2005)	Priority date ( <i>day/month/year</i> ) 18 February 2004 (18.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant YAMAGAMI, Satoru		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).
  2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:
 

<input checked="" type="checkbox"/> Box No. I	Basis of the report
<input type="checkbox"/> Box No. II	Priority
<input type="checkbox"/> Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/> Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/> Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/> Box No. VI	Certain documents cited
<input type="checkbox"/> Box No. VII	Certain defects in the international application
<input type="checkbox"/> Box No. VIII	Certain observations on the international application
4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Date of issuance of this report 19 September 2006 (19.09.2006)
Facsimile No. +41 22 338 82 70	Authorized officer <div style="text-align: center; font-weight: bold;">Yoshiko Kuwahara</div> e-mail: pt07@wipo.int

# PATENT COOPERATION TREATY

TRANSLATION

From the  
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:		Date of mailing (day/month/year)
Applicant's or agent's file reference <b>A55037H</b>		<b>FOR FURTHER ACTION</b> See paragraph 2 below
International application No. <b>PCT/JP2005/002402</b>	International filing date (day/month/year) <b>17.02.2005</b>	Priority date (day/month/year) <b>18.02.2004</b>
International Patent Classification (IPC) or both national classification and IPC		
Applicant <b>YAMAGAMI, Satoru</b>		

**1. This opinion contains indications relating to the following items:**

- |                                     |              |  |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion   |
| <input type="checkbox"/>            | Box No. II   | Priority   |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability   |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention   |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited  |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application   |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application  |

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2005/002402

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language  
\_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/JP2005/002402

**Box No. V** Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability:  
citations and explanations supporting such statement

**1. Statement**

Novelty (N)	Claims	3, 5, 9, 14-15	YES
	Claims	1-2, 4, 6-8, 10-13	NO
Inventive step (IS)	Claims		YES
	Claims	1-15	NO
Industrial applicability (IA)	Claims	1-15	YES
	Claims		NO

**2. Citations and explanations:**

**Document 1**

✓ Shiro AMANO, et al., Me no Saisei Igaku, Kakumaku Naihi Saibo Ishoku  
Journal of Japanese Ophthalmological Society (2002), Vol. 106, No. 12, p. 805-836

**Document 2**

✓ JP 2002-078723 A (Hoya Healthcare Corp.) 19 March 2002, Full text (Family: none)

Based on the description in document 1 cited in the international search report, the inventions of claims 1, 2, 4, 6-8, and 10-13 lack novelty and an inventive step.

Document 1 describes the preparation of a transparent collagen sheet using collagen that has been alkali-solubilized from animal dermis, and it states that even when this transparent collagen sheet was transplanted to rabbit cornea, the transparency thereof was maintained.

In addition, document 1 states that when human corneal endothelial cells are cultured on this collagen sheet after an ECM, which is an extracellular matrix of bovine corneal endothelial cells, was formed, the corneal endothelial cells on the collagen sheet formed a cellular monolayer, and that using this collagen sheet it is possible to prepare cultured corneal endothelium and a reconstructed cornea.

In addition, document 1 states that as conditions when culturing the corneal endothelial cells on a substrate and forming a reconstructed cornea, cellular density was increased and cellular adhesion was promoted by inoculating the substrate with a liquid containing subcultured 5th passage corneal endothelial cells at a concentration of  $5 \times 10^4$  cells/2 mL.

This being the case, this authority finds that the inventions of claims 1, 2, 4, 6-8, and 10-13 are indistinguishable from the invention described in document 1.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2005/002402

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V.

Based on the description in document 1 cited in the international search report, the invention of claim 3 lacks an inventive step.

Because applying an adhesion factor or biological adhesive to the surface of a culture vessel to increase the adhesion of cell layers and sheets of biological material is a widely known and conventionally practiced means, this authority finds that persons skilled in the art can easily conceive of applying an adhesion factor or biological adhesive to the surface of the culture vessel and the like to provide an adhesion factor or biological adhesive on the opposite surface of the collagen sheet to the cultured layer of corneal endothelial cells.

Based on the descriptions in documents 1 and 2 cited in the international search report, the inventions of claims 5, 9, and 14-15 lack an inventive step.

Document 1 describes the culturing of corneal endothelial cells using a cell culture liquid medium wherein fetal calf serum and growth factors are added to a medium with a low glucose concentration.

Document 2 describes a process for reconstructing a cornea wherein corneal epithelial cells subcultured for 2 to 10 passages are cultured a corneal substrate, and it states that the corneal endothelial cells are cultured under conditions of 37°C and 10% CO<sub>2</sub>, and they are cultured in a cell culture liquid medium wherein fetal calf serum, growth factors, and hyaluronic acid are added to a medium with a low glucose concentration. In addition, document 2 states that when an adhesion factor such as human fibronectin and the like is bound to the corneal substrate, the endothelial cell adhesion efficiency increases, and therefore such a procedure is preferred.

Documents 1 and 2 belong to a common technical field because they are both processes for reconstructing a cornea by culturing corneal endothelial cells on a substrate. Therefore, this authority finds that based on the description in document 2, persons skilled in the art can easily conceive of using human fibronectin in place of ECM on the collagen sheet used as a substrate and can culture corneal endothelial cells under conditions of 37°C and 10% CO<sub>2</sub> in the invention described in document 1, and they can also perform culturing using a cell culture liquid medium wherein hyaluronic acid is added to the medium of the invention described in document 1.